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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,366	11/21/2001	George Jackowski	2132.101	5753

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EXAMINER
DAVIS, DEBORAH A

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/15/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,366	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Deborah A Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-2) in Paper No. 11 is acknowledged. The traversal is on the ground(s) that Sequence ID 1-3 should be joined together because they are fragments of same type of apolipoprotein and share common utility as markers. The traversal is also on the ground ***In re Ochiai*** practice of rejoining claims that are found to be allowable subject matter. This is not found persuasive because although they are constructed from the same apoliprotprotein, each protein is considered independent and distinct inventions as evidenced by their different SEQ ID No's 1, 2 and 3. Although they are constructed from the same apoliproprotein, once isolated, they are considered independent and distinct structures. Further, nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

2. Applicant has cancelled claims 2-38 and has added new claims 39-46. Claims 1 and 39-46 are currently under consideration for examination.

Specification

3. (g) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74. There is no description of Figures 2 and 3 in the specification. Please correct.

Drawings

4. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 1 is directed to non-statutory subject matter. The invention as claimed read on any biopolymer making having SEQ ID NO:1, wherein the protein molecule includes products of nature. Non-naturally occurring compositions are considered to be patentable subject matter within the scope of 35 U.S.C. 101. Compositions that are products of nature are considered non-statutory and non-patentable. See Official Gazette, 1077 O.G. 24, April 21, 1987. It is recommended that the claims incorporate the claim language, "isolated" or "purified" to overcome this rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 39-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to a biopolymer marker peptide consisting of SEQ ID NO:1 diagnostic for insulin resistance, methods of using and a kit.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factor to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention – the invention is directed to a biopolymer marker peptide for insulin resistance, method and kit of using said marker consisting of SEQ ID NO:1.

The state of the prior art – the prior art of record fails to disclose a biopolymer marker peptide for insulin resistance, method and kit consisting of SEQ ID NO:1.

The predictability or lack thereof in the art – there is no predictability based on the instant specification that the protocol for making SEQ ID NO:1, 2 or 3 would work. The instant specification fails to demonstrate how the recited protocols (see pages 40-46) would result in SEQ ID NO's 1-3 further these protocols do no clearly explain what procedure or process is being taught.

The amount of direction or guidance present – The specification fails to provide any clear guidance to one of ordinary skill in the art to reproduce SEQ ID NO's 1-3 with undue experimentation.

The presence or absence of working examples – Figure 1 is provided in the specification as a working example, however SEQ ID NO's 1-3 are absent as markers for insulin resistance. Further, the control data is vague and confusing because it contains other proteins without explaining the relevance to SEQ ID NO's 1-3.

The quantity of experimentation necessary – it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

The relative skill of those in the art – the level of skill in the art is high.

The breadth of the claims – as recited, the instant claims are directed to a biopolymer marker peptide for insulin resistance consisting of SEQ ID NO: 1. The claims are also directed to a method and kit consisting of SEQ ID NO: 1.

While the specification gives examples of protocols and recites that SEQ ID: NO's 1-3 would be the end result (page 46) it is unclear as to how the protocol would make each SEQ ID peptide. There is no example provided of a starting protein subsequent fragmentation that would result in the peptides of the said SEQ IDs, only the recitation of reagents used. Applicant also recites that Syndrome X is related to cardiovascular condition, high blood pressure; obesity which applicant says eventually leads to a disease state such as diabetes, kidney failure and heart failure. One skilled in the art would know that high blood pressure, high fat levels in the blood and obesity can lead to such disease states, but the specification has not demonstrated hat SEQ ID NO: I is a marker for Syndrome X. Although samples have been taken from a patient at different points and times, the data is only representative of a single patient, and further, applicant has not has not demonstrated that data from this patient was compared to a

normal patient, it was only compared to the structure of SEQ ID: NO's 1-3. Therefore how is it determined that high or low levels of SEQ ID NO:1-3 is indicative of a disease state or the onset of a disease, namely insulin resistance.

Tockman et al. (Cancer Research 52 :27 :2711-2718, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other **insulin biomarkers**. Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, established quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of pre-clinical cancer and **if validated,** can be used for population screening (page 2714, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological conformation of disease. "This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]" (see page 2714, column 1) Biomarker Validation against Acknwledged Disease End Points section. Clearly, prior to the successful

application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies with a population with a disease or disorder is highly speculative and unpredictable.

Therefore, in view of the insufficient guidance in the specification, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (703) 308-4427. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

Deborah A. Davis
CM1, 7D116
July 11, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
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07/14/03